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Is Weight Lifting Effective in Reducing Lymphedema in Breast Cancer Survivors?

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ABSTRACT

OBJECTIVE: The objective of this selective EBM review is to determine whether or not weight lifting is effective in reducing lymphedema in breast cancer survivors.

STUDY DESIGN: Systematic review of three English language primary studies published in 2009 and 2010.

DATA SOURCES: Three single blind, randomized controlled trials comparing progressive weight lifting and other treatments in breast cancer survivors were found using the Cochrane Database of Systematic Reviews and PubMed.

OUTCOMES MEASURED: Incidence of breast cancer-related lymphedema onset measured by blinded certified lymphedema therapists using a standardized clinical evaluation derived from the Common Toxicity Criteria version 3.0, comprising of interlimb differences, patient symptoms, and variation in arm tissue tone or texture. Incidence of lymphedema exacerbations measured by blinded certified lymphedema specialists using a standardized evaluation. Number and severity of lymphedema symptoms measured through participant-reported validated surveys evaluating the occurrence and severity of 14 lymphedema-related arm symptoms: rings too tight, watch too tight, bracelet too tight, clothing too tight, puffiness, knuckles or veins not visible, leathery skin, tired arms, pain, pitting, swelling after exercise, difficulty writing, or other. Pain and heaviness sensation in affected arm measured with the visual analogue scale (VAS). Change in arm and hand swelling determined by water volume displacement.

RESULTS: Sagen et al (2009) did not find weight lifting to be effective in reducing lymphedema onset in breast cancer survivors. Schmitz et al (2009) did find a significant relationship between weight lifting and reduced lymphedema exacerbations when considering evaluations by certified specialists and patient-reported validated surveys. Schmitz et al (2010) did not show a significant relationship between weight lifting and reduced lymphedema when using clinician-defined lymphedema onset.

CONCLUSIONS: The studies in this review provide inconclusive evidence in determining whether weight lifting is effective in reducing lymphedema in breast cancer survivors. Future RCTs are needed to evaluate the efficacy of weight lifting and lymphedema.

KEY WORDS: Exercise, weight lifting, lymphedema, breast cancer

INTRODUCTION

Lymphedema is a debilitating disorder and frequently feared consequence of breast cancer treatment. The fundamental issue is lymphatic dysfunction in which proteins, lipids and water cannot be brought back to the intravascular space, causing abnormal buildup of interstitial fluid [1]. Upper extremity lymphedema often causes patients to restrict the use of their affected limb in the hopes of preventing or reducing symptoms, such as swelling, heaviness, and pain [2]. However, limited use of the arm may actually increase the chance of injury and lymphedema [3].

Lymphedema is a major concern among breast cancer survivors and health care providers because it is a chronic and progressive disorder. It specifically causes physical problems, emotional stress, and a significant impact on quality of life. Currently, there are over 2.4 million breast cancer survivors in the Unites States, with nearly 184,000 American women diagnosed with breast cancer yearly [2]. About 61% of breast cancer patients have sentinel lymph node biopsy performed, with 5-7% forming lymphedema. Furthermore, one-third of breast cancer patients undergo complete axillary dissection, with lymphedema developing in 13-47% [3].

Research shows that women with breast cancer-related lymphedema have considerably higher two-year, post-operative medical costs than breast cancer patients without lymphedema. The rise in cost ranges from $14,877 to $23,167, and is due to office visits, prescription medication, treatment for infections, mental health services, and diagnostic testing. These patients also experience more interrupted days for hospitalization or office visits at 58.7 days within two years, compared to 46.5 days within two years for survivors without lymphedema [4].

Currently, there is no known cure for lymphedema [4]. However, what is known about this high-protein edematous disorder is that the interstitial high oncotic pressure state promotes further buildup of water. As a result, the surrounding outflow tracts significantly dilate, valves

become nonfunctional, and lymphatic walls turn fibrotic. An inflammatory reaction takes place, leading to major risk of chronic infection, as well as the distinguishing change from initial pitting edema to nonpitting lymphedema [1]. There are many risk factors for upper extremity lymphedema, including breast cancer treatment with axillary node dissection, chemotherapy, and breast or axillary radiation, as well as high BMI, injuries, infections, increased amount of lymph nodes affected by the tumor, and surgical intervention on the dominant or non-dominant limb [4,5].

Lymphedema treatment includes symptom relief, proper skin hygiene, manual lymphatic drainage, elastic compression garments, pneumatic pumps, multilayer bandaging, and palliative surgical therapy [1,4]. Although research indicates that exercise is beneficial for breast cancer survivors and holds no increased risk of lymphedema, health care providers frequently encourage physical activity restrictions of the affected extremity during rehabilitation [5]. Since restricting upper extremity movement may hinder recovery and decondition the arm, weight lifting may enhance physical-work ability and protect the limb during routine daily activities. It is theorized that progressive weight lifting either combined with or used as an alternative to current therapy may reduce the onset of lymphedema symptoms and incidence of exacerbations [2,3].

OBJECTIVE

The objective of this selective EBM review is to determine whether or not weight lifting is effective in reducing lymphedema in breast cancer survivors.

METHODS

Included in this analysis were three single blind, randomized controlled trials (RCTs) all of which compared weight lifting to other treatments. The population studied was female breast cancer survivors. The intervention used was progressive weight lifting and the comparison was either no weight lifting or change in baseline exercise level, or activity restrictions combined

with usual care program without a weight lifting intervention. To measure outcomes, various methods were used including lymphedema onset and diagnosis, change in arm and hand swelling, incidence of lymphedema exacerbations, and number and severity of symptoms.

A detailed inquiry was performed by the author of this review between December 2010 and February 2011 using the Cochrane Database of Systematic Reviews and PubMed. The key words "exercise," "weight lifting," "lymphedema," and "breast cancer" were used in combinations to search for articles. The RCTs chosen were published in English and in peer-review journals from 2009-2010. Articles were selected based on their relevance and the importance of outcomes to the patient (Patient Oriented Evidence that Matters, or POEMs). Studies included in this review were three RCTs published after 1996, all of which included patient oriented outcomes. The exclusion criteria consisted of male patients, participants under age 18, breast cancer patients who did not undergo lymph node dissection, or regimens that did not involve upper body progressive weight training. The statistics utilized were relative risk reduction (RRR), absolute risk reduction (ARR), relative benefit increase (RBI), absolute benefit increase (ABI), number needed to treat (NNT), 95% confidence interval, and p-value. Table 1 represents the demographics and characteristics of included studies.

Table 1- Demographics & characteristics of included studies [2,3,5]

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Sagen, 2009	RCT	207	32-75 (mean-55)	Women w/ Hx of early-stage breast ca & mastectomy or breast-conserving surgery with axillary node dissection, with or without radiotherapy, chemotherapy, or hormone therapy	Age > 75 yrs, difficulty understanding Norwegian, and presence of metastasized breast cancer, other types of cancer, injury, poor functioning of upper limb	3	No activity restrictions (NAR) in daily living combined with a moderate resistance exercise program for 6 months
Schmitz, 2009	RCT	141	Age ≥ 18 (mean-56; 58)	Women w/ Hx of unilateral non-mets breast ca dx 1-15 yrs before study entry, BMI	Hx of B/L ca, current ca, moved away, no LN removed, received dx w/in	11	One-year progressive weight lifting regimen

				≤ 50kg/m^2, no current evidence of ca, no medical conditions limiting exercise, ≥ 1 LN removed, clinical dx of stable breast ca-related lymphedema	previous yr or > 15 yrs before study entry, medical contraindication, currently weight lifting or enrolled in weight loss program, did not have lymphedema		
Schmitz, 2010	RCT	154	36-75 (mean-54; 56)	Women w/ Hx of U/L non-mets breast ca dx 1-5 yrs before study entry, BMI ≤ 50kg/m^2, cancer free, no medical conditions limiting exercise, no plans for surgery or to be away ≥ 1 month, ≥ 2 LN removed, no prior dx of lymphedema, currently no lymphedema	Hx of B/L ca, current ca, moved away, < 2 nodes removed, dx w/ in 1 yr or >5 yrs before study entry, medical contraindication, currently weight lifting or enrolled in weight loss program, had lymphedema	20	One-year progressive weight lifting regimen

OUTCOMES MEASURED

The main outcome for Sagen et al (2009) was Voldiff (in ml) or the volume difference of the affected and control arms using the Simplified Water Displacement Instrument. The other primary outcome included pain and heaviness sensation in the affected arm during physical activity using the visual analogue scale (VAS) [5]. The outcomes measured by Schmitz et al (2009) consisted of frequency of lymphedema exacerbations determined by blinded certified lymphedema specialists using a standardized evaluation, as well as number and severity of lymphedema symptoms measured through participant-reported validated surveys evaluating the occurrence and severity of 14 lymphedema-related arm symptoms (rings too tight, watch too tight, bracelet too tight, clothing too tight, puffiness, knuckles or veins not visible, leathery skin, tired arms, pain, pitting, swelling after exercise, difficulty writing, or other). The authors also examined difference in arm and hand swelling at one year, comparing the affected and unaffected arms through displaced water volume [2]. The main outcome for Schmitz et al (2010) was clinician-defined breast cancer-related lymphedema onset measured by blinded certified

lymphedema therapists using a standardized clinical evaluation derived from the Common Toxicity Criteria version 3.0, comprising of interlimb differences, patient symptoms, and variation in arm tissue tone or texture. The authors also measured lymphedema onset as 5% or greater increase in arm swelling through water volume displacement [3].

RESULTS

All three studies were RCTs in which the outcome assessors, clinicians and study workers were kept blind. The exercise intervention for all three experiments took place at outpatient clinics or fitness centers. In the experiment performed by Sagen et al (2009), a portion of the results was reported in dichotomous format, with the rest as continuous data. Results reported by Schmitz et al (2009) and Schmitz et al (2010) were presented in dichotomous format.

Sagen et al (2009) found that at two years post surgery, 13% of both the no activity restriction (NAR) group and activity restriction (AR) group had arm lymphedema (87% of both NAR and AR groups without lymphedema onset). The RRR and ARR were both calculated to be 0%. NNT was determined to be 0, indicating that the outcome was random, with no relation between weight lifting and reduced lympedema onset (Table 2). The Voldiff (in ml) at two years for NAR and AR were not significantly different, with mean measurements of NAR at 52 ml (± 153) and AR at 82 ml (± 165). The VAS ratings of pain and sensation of heaviness for NAR and AR were not significantly different at two years after surgery (p-value > 0.05). Regarding the NAR participants, 61% had no pain, 24% experienced pain between 1 and 20mm, and 15% had pain above 21mm. For the AR group, 64% had no pain, while 17% experienced pain between 1 and 20mm and 17% had pain greater than 21mm on the VAS at two-year follow-up (Table 3) [5].

Table 2- Efficacy of weight lifting in prevention of lymphedema [3,5]

Study	CER	EER	RRR	ARR	NNT	95% CI	p-value
Sagen, 2009	87%	87%	0%	0%	0	N/A	N/A
Schmitz, 2010	95.6%	98.5%	0.03%	2.9%	35	0.04-3.22	0.12

Table 3- Visual analogue scale (VAS) ratings of pain and heaviness in affected limb for NAR and AR at two-year follow-up for Sagen et al (2009)

VAS	No Pain, 0 mm	Pain, 1-20 mm	Pain, > 21mm
NAR	61%	24%	15%
AR	64%	17%	17%

Schmitz et al (2009) reported a lower incidence of lymphedema exacerbations for the weight lifting group at 14%, compared to the control group at 29% as determined by the certified lymphedema specialists using standardized evaluations (86% of the weight lifting group and 71% of the control group without lymphedema exacerbations). The difference in frequency of lymphedema exacerbations was statistically significant with a 95% confidence interval of 0.23 to 0.97 and p-value of 0.04. The RBI was calculated to be 0.211%, the ABI was 15%, and NNT was 7. This NNT value indicates that for every seven patients who followed the weight lifting treatment, there was one fewer incidence of lymphedema exacerbations compared to control (Table 4). The authors also found that the percentage of participants who had an increase in limb swelling by 5% or greater were statistically similar between the weight lifting and control groups. About 11% of the weight lifting group and 12% of the control group had an increase in limb swelling by 5% or more, with a 95% confidence interval of 0.88 to 1.13 and p-value of 1.00. Furthermore, Schmitz et al (2009) determined that the weight lifting group had significantly greater improvements in severity of lymphedema symptoms as measured through self-reported validated surveys, with a 95% confidence interval of -0.54 to -0.03 and p-value of 0.03. However, the difference between the two groups regarding change in the number of symptoms measured through the self-reported validated surveys was not statistically significant, with a 95% confidence interval of -1.32 to 0.06 and p-value of 0.07 (Table 5) [2].

Table 4- Efficacy of weight lifting in treatment of lymphedema [2]

Study	CER	EER	RBI	ABI	NNT	95% CI	p-value
Schmitz, 2009	71%	86%	0.211%	15%	7	0.23–0.97	0.04

Table 5- Change in severity and number of lymphedema symptoms between weight lifting and control groups through self-reported validated surveys for Schmitz et al (2009)

Variable	95% CI	p-value
Change in severity of symptoms, weight lifting vs. control	-0.54- -0.03	0.03
Change in number of symptoms, weight lifting vs. control	-1.32- 0.06	0.07

Schmitz et al (2010) reported that the percentage of participants who had clinician-defined breast cancer-related lymphedema onset was similar between the weight lifting and control groups. About 1.5% of the weight lifting group and 4.4% of the control had clinician-defined onset (98.5% of the weight lifting group and 95.6% of the control group without lymphedema onset). The difference between these two groups was not statistically significant with a 95% confidence interval of 0.04 to 3.22 and p-value of 0.12. The RRR was calculated to be 0.03% and ARR was 2.9%. NNT was determined to be 35, indicating that for every 35 patients who followed the weight lifting treatment, there was one fewer incidence of lymphedema onset compared to control (Table 2). The authors also found that the percentage of participants who had an increase in limb swelling by 5% or greater were statistically different between the weight lifting and control groups. There was a lower incidence of lymphedema onset for the weight lifting group at 11%, compared to the control at 17%, as determined by water volume displacement. The difference in frequency of lymphedema onset was statistically significant with a 95% confidence interval of 0.28 to 1.45 and p-value of 0.003. Schmitz et al (2010) performed a secondary analysis restricted to participants with 5 or more lymph nodes removed. The authors reported that about 2.4% of the weight lifting group and 6.5% of the control had clinician-defined lymphedema onset. The difference between these groups was not statistically significant with a 95% confidence interval of 0.04 to 3.38 and p-value of 0.13. They also found a lower incidence of lymphedema onset for the weight lifting group at 7%, compared to the control at 22%, defined as 5% or greater increase in arm swelling determined by water

volume displacement. The difference in frequency of lymphedema onset was statistically significant with a 95% confidence interval of 0.09 to 1.00 and p-value of 0.001 (Table 6) [3].

Table 6- Lymphedema onset in patients with ≥ 5 lymph nodes removed for Schmitz et al (2010)

	Weight Lifting	Control	95% CI	p-value
≥ 5% increase in arm swelling	7%	22%	0.09-1.00	0.001
Clinician-defined onset	2.4%	6.5%	0.04-3.38	0.13

The included studies required a history of nonmetastatic breast cancer in women. Participants in the study by Sagen et al (2009) were randomized into either the no activity restrictions (NAR) group with moderate resistance exercise training for six months or the control group with physical activity restrictions (AR) of the affected limb for six months. The AR participants were instructed to refrain from strenuous physical activities or lifting objects with a weight greater than 3kg. The study began with 207 participants with a clinical diagnosis of breast cancer and complete axillary node dissection. Two women were excluded because they were found to not have node dissection and one woman was excluded because her baseline measurements were unintentionally deleted from the databank. There were 52 missing participants at the two-year follow-up for several reasons: 14 women died, three moved to another location, 13 could not be contacted with the provided information, seven refused to participate, four were too frail or ill to continue, two control participants had axillary node dissection, and nine were lost to follow-up for reasons not mentioned. Program adherence for the NAR group was 83% with a mean duration of attendance at 21 ± 4.8 weeks, while program adherence for the AR group was 89% with a mean duration of attendance at 22 ± 5.2 weeks [5].

For Schmitz et al (2009), the participants were randomized into either a one-year progressive weight lifting regimen or a control group in which participants were instructed to maintain their baseline exercise level. The study began with 141 participants with a diagnosis of stable breast cancer-related lymphedema. Nine women were lost to follow-up and two withdrew

due to a second primary or recurrent cancer. The median attendance rates for the weight lifting intervention in the first, second, third and fourth quarters were 96%, 88%, 81%, and 75% [2].

Participants in the study by Schmitz et al (2010) were randomized into either a one-year progressive weight lifting regimen or a control group in which participants were asked not to alter baseline level of exercise during the study. The study began with 154 participants at risk for lymphedema at baseline, with 13 women lost to follow-up and 7 withdrawing due to recurrent cancer. The median attendance of the weight lifting group was 79%, including those lost to follow-up. Schmitz et al (2010) included a special subset analysis of women with 5 or more lymph nodes removed to remain uniform with their earlier research and because majority of published research consists of sentinel lymph node biopsies with resection of 1 to 4 nodes [3].

In the experiment performed by Sagen et al (2009), adverse events took place in three out of 104 participants from the intervention group: "two participants developed adhesive capsulitis with progressive immobilization and one patient developed supraspinatus tendinopathy." The authors take note of the high possibility that one of these patients had latent frozen shoulder just prior to study entry [5]. Schmitz et al (2009) denied any serious adverse events related to the weight lifting intervention, and Schmitz et al (2010) did not report adverse events.

DISCUSSION

The Position Statement of the National Lymphedema Network in December 2011 provides an update regarding lymphedema and exercise. The organization states that lymphedema patients may participate in progressive weight lifting exercises through lifting body weight or objects with caution, in either an isometric or isotonic manner. The guidelines recommend that patients begin with lighter weights, lower number of repetitions, and gradual progression in intensity. The organization advises that patients should consult with a qualified

lymphedema specialist and personal trainer, allow enough time for rest in between sets, avoid weights that may constrict the limb, wear compression garments during exercise, stay hydrated, avoid overheating, and rotate which body parts are being worked during a session [6]. Prior research has shown that both physical activity and the associated rise in pulmonary effort increases lymph flow and enhances protein resorption. Also, greater muscle strength may lower the impact of daily stresses to the affected extremity. Other positive factors regarding progressive weight lifting include its wide availability at community fitness centers throughout the United States and its affordability. However, it is important to acknowledge that the National Lymphedema Network 2005 guidelines stated that strength training is a form of exercise holding the highest risk to lymphedema patients [2]. Although recent research has demonstrated the healthy effects of exercise on lymphedema patients, many health care providers still recommend limited activity of the affected extremity as a precaution against developing lymphedema [5].

The study by Sagen et al (2009) did not show a significant relationship between weight lifting and reduced lymphedema onset in breast cancer survivors. The data found by Schmitz et al (2009) suggest a significant relationship between weight lifting and reduced lymphedema exacerbations when considering evaluations by certified specialists and patient-reported validated surveys. However, the relationship was not significant when using the gold standard of water displacement. The experiment by Schmitz et al (2010) did not show a significant relationship between weight lifting and reduced lymphedema when using clinician-defined lymphedema onset. However, there was a significant relationship between weight lifting and reduced onset of lymphedema when using the gold standard of measuring water displacement.

A major limitation, which applied to each study, was that the participants could not be blinded due to the fact that they knew whether or not they were in the weight lifting group. This

fact posed a risk for accidental disclosure of which group a patient belonged to. Another limitation for Sagen et al (2009) was the number of participants lost at the two-year follow-up: 36 in the NAR group and 16 in the AR group. A potential weakness specifically mentioned in the experiment by Schmitz et al (2009) is that the lymphedema exacerbations were examined by six certified therapists, rather than just one, which leaves room for inconsistency. Another limitation is that the intervention participants may have revealed their recent weight lifting during evaluations for possible exacerbations, resulting in biased assessments. A potential limitation in the experiment by Schmitz et al (2010) is that the intervention group participants may have disclosed their recent exercise during the evaluation sessions for lymphedema onset.

All three experiments demonstrated strengths such as high adherence rates, as previously mentioned. Additionally, each intervention took place over a relatively longer period of time. Lastly, although the trials looked at different patient oriented outcomes, each study also used the gold standard of displaced water volume to evaluate lymphedema.

CONCLUSION

The studies in this review provide inconclusive evidence in determining whether weight lifting is effective in reducing lymphedema in breast cancer survivors. Future studies are needed to evaluate the efficacy of weight lifting and lymphedema. Since there were variations in the methods reviewed, future trials should use a larger sample size, examine weight lifting alone as the intervention without the combination of other modalities, and follow a control that requires no change in the individual's baseline. Also, efforts should be made to use a weight lifting regimen that is standardized in the gradual progression and frequency of exercise. However, studies are currently underway to determine the relationship between lymphedema treatment and the impact on symptoms and quality of life [7].

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